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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,694	05/01/2006	Wolfgang Kreisel	64609(70301)	3005

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EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
STONE, CHRISTOPHER R	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
08/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,694	KREISEL, WOLFGANG	
	Examiner	Art Unit	
	CHRISTOPHER R. STONE	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *5-7 and 13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed April 30, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Election/Restrictions

Claims 5-7 and 13-16 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim (see p. 2 of the Office Action mailed January 31, 2008). Claims 5-7 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, i.e. Applicant elected bleeding complications of portal hypertension as the species of disease of condition from the list in claims 2 and 5 (see p. 4 of the Requirement for Restriction mailed October 26, 2007).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of portal hypertension and its bleeding complications, does not reasonably provide enablement for the prevention of portal hypertension and its bleeding complications. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 1-4 and 8-12 are drawn to a method of treating and preventing portal hypertension and associated conditions and complications comprising administering a PDE 5 inhibitor. Vardenafil and bleeding complications of portal hypertension are the elected species of PDE 5 inhibitor and disease condition related to portal vein pressure currently under examination. The prior art teaches that portal hypertension and its bleeding complications are difficult to treat, and that there is no known prevention. For instance, de Franchis et al teaches that all patients with cirrhosis of the liver will eventually develop portal hypertension and esphagogastric varices (abstract). This indicates a lack of predictability of preventing portal hypertension in the art. Furthermore, the Applicant has provided no working example demonstrating the ability of this method to prevent portal hypertension and has provided no direction on how to carry out the method of preventing portal hypertension. For these reasons, it would take undue experimentation for one of ordinary skill in the art to practice the prevention of portal hypertension with a reasonable expectation of success.

Applicant argues that an effective prevention of portal hypertension is provided in the instant Application. This is an allegation without factual support and is therefore unpersuasive. As noted above, the prior art teaches that portal hypertension and its bleeding complications are difficult to treat, and that there is no known prevention. This indicates a lack of predictability of preventing portal hypertension in the art. Furthermore, the Applicant has provided no working example demonstrating the ability

of this method to prevent portal hypertension and has provided no direction on how to carry out the method of preventing portal hypertension. For these reasons, it would take undue experimentation for one of ordinary skill in the art to practice the prevention of portal hypertension with a reasonable expectation of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garcia et al in view of Garcia-Tsao (both references provided by Applicant), further in view of Niazi et al (US Patent 6338862).

Claims 1-4 and 8-12 are drawn to a method of treating portal hypertension comprising administering a PDE 5 inhibitor. Vardenafil and bleeding complications of portal hypertension are the elected species of PDE 5 inhibitor and disease condition related to portal vein pressure currently under examination.

Garcia teaches that administration of the PDE 5 inhibitor, Sildenafil, at 10 mg/kg body weight, decreases portal vein pressure (abstract). Garcia does not teach the use of the PDE 5 inhibitor Vardenafil, or that the PDE 5 inhibitor induced decrease in portal vein pressure treats bleeding complications of portal hypertension. Niazi teaches that Vardenafil is a known PDE 5 inhibitor (column 4, lines 57-61). Garcia-Tsao teaches that portal hypertension is the cause of gastroesophageal varices and variceal hemorrhage

(abstract). Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to use, Vardenafil, in place of Sildenafil, since they have PDE 5 inhibitory activity, known to cause a decrease in portal vein pressure, to treat portal hypertension and the known complications of portal hypertension, gastroesophageal varices and variceal hemorrhage in humans. Thus, resulting in the practice of the instantly claimed invention with a reasonable expectation of success. Additionally, it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to administer Vardenafil in a single oral dosage form, since this method of administration is common in the pharmaceutical art.

Applicant argues that Garcia does not deal with the treatment of portal hypertension. This is found unpersuasive because Garcia explicitly teaches that 10mg/kg Sildenafil was associated with a 16.5% decrease in portal vein pressure (abstract, lines 24 and 25), motivating one of ordinary skill in the art to treat portal hypertension with a PDE 5 inhibitor as noted above. Applicant argues that the 10mg/kg dosage of Sildenafil resulted in an unsafe drop in systemic blood pressure. This is an allegation without fact and is therefore unpersuasive. Applicant has provided no evidence that the effect on systemic hypertension would prevent one of ordinary skill in the art from using the dosage of Garcia. Additionally, a decrease in systemic blood pressure may also be desired in a patient with severe hypertension. Applicant further argues that does not teach the selective activity of a PDE 5 inhibitor on portal vein flow versus arterial vein flow into the liver. This selective activity is a characteristic of the

method rendered obvious by the prior art, as noted above. This activity flows from a property of Vardenafil and is necessarily present in the prior art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

28July2008
CRS

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614